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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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MINTZ, LEVIN, COHN, FERRIS, GLOVSKY
AND POPEO, P.C.
ONE FINANCIAL CENTER
BOSTON, MA 02111

EXAMINER	
FALK, ANNE MARIE	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 11/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/693,043	BJORKLUND, ANDERS	
	Examiner	Art Unit	
	Anne-Marie Falk, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6,13 and 14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 6, 13, and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed August 24, 2005 (hereinafter referred to as "the response") has been entered. Claims 1 and 3 have been amended.

Accordingly, Claims 1-3, 6, 13, and 14 remain pending in the instant application.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 24, 2005 has been entered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

New Matter

Claims 1-3, 6, 13, and 14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The amended claims include new matter.

As amended, Claim 1 recites transplanting "at least about $1x10^6$ mitogenic growth factor-responsive neural stem cells." However, the specification does not contemplate transplanting "at least about $1x10^6$"cells. At page 4 of the response, Applicants assert that support for the number of transplanted neural stem cells can be found in the specification at page 14, lines 4-5, which states that "a density of about 10,000-1,000,000 cells per μl, preferably 25,000 to-500,000 cells per μl, is preferred for transplantation" and at page 15, lines 15-17, which states that "multiple deposits of cell sphere suspensions may be made, for example 500,000 cells per deposit, in the striatum of the brain." Applicants further refer to support at page 31, lines 22-25, which states that "each rat received six deposits of 0.3 μl sphere suspension, equivalent to approximately 500,000 cells ..." Applicants conclude that since the specification contemplates an upper cell density of 1,000,000 cells per μl, and teaches that multiple deposits can be made, for example 6, recitation of **$6x10^6$** cells transplanted to a host subject presents no new matter (page 4, paragraph 1 of the response). Contrary to Applicants' assertion, the claims do not recite transplanting **$6x10^6$** cells. Rather the claims recite transplanting "at least about $1x10^6$" cells. The section cited by Applicants at page 31, lines 22-25 (Example 15) clearly discloses that **500,000 cells** were transplanted into each rat. Thus, it is clear that this example does **not** provide support for transplanting "at least about $1x10^6$" cells, as now recited in the claims, and in fact is contrary to the suggestion that "at least about $1x10^6$"cells should be used. Example 15 states that a cell suspension at a "final concentration of 250,000 cells/μl" was used (page 31, line 12). The specification then states, at page 31, lines 22-25, as cited by Applicants, that "each rat received six deposits of 0.3 μl sphere suspension, **equivalent to approximately 500,000 cells** ..." (emphasis added). Indeed, a cell suspension at a final concentration of 250,000 cells/μl delivered in six aliquots of 0.3 μl each is 450,000 cells (250,000 cells/μl x 0.3 μl x 6 deposits = 450,000 cells), which is **equivalent to approximately 500,000 cells** as stated in the specification. This does not provided support for "at least about $1x10^6$"

cells, as now recited in the claims. Nowhere does the specification contemplate administering "at least about $1x10^6$" cells.

Further, in response to Applicants' contention that "the specification contemplates an **upper** cell density of 1,000,000 cells per μl" (emphasis added; see page 4 of the response, paragraph 1, line 10), it is unclear how an **upper limit** can provide support for a **lower limit.** The claims recite a **lower limit** of "at least about $1x10^6$" cells with **no** upper limit. It is clear that the specification does **not** contemplate a lower limit of "at least about $1x10^6$" cells, because the examples themselves use less than $1x10^6$ cells. Example 8 discloses the administration of "a total of about 250,000-500,000 cells" (page 25, line 23 of the specification) and Example 9 discloses the transplantation of approximately 300,000 neural stem cells into the striatum of adult rats (page 26, line 3). Example 15 discloses the administration of approximately 500,000 cells (page 31, lines 23-24) into the striatum of adult rats. Nowhere does the specification contemplate administering "at least about $1x10^6$" cells.

Thus, the amended claims include new matter.

As amended, Claim 1 recites "said first area comprising multiple loci for receiving an aliquot of the neural stem cells" which constitutes new matter. Applicants have not pointed to any support for the newly added claim limitation and the Examiner has reviewed the entire disclosure and does not find support in the as-filed specificaton. The specification only contemplates a first locus and a second locus, but does not contemplate a "first area comprising multiple loci." See, for example, page 3, lines 10-17, which refers to a first locus and a second locus. Furthermore, the specification does not contemplate transplanting the neural stem cells to multiple loci. Rather, the specification contemplates "multiple deposits" as set forth at page 15, line 16, but does not contemplate "multiple loci" nor a "first area comprising multiple loci."

Thus, the amended claims include new matter.

Enablement

Claims 1-3, 6, 13, and 14 stand rejected under 35 U.S.C. 112, first paragraph, for reasons of record advanced on pages 3-5 of the Office Action mailed 2/23/05, on pages 3-7 of the Office Action mailed 6/3/04, on pages 2-9 of the Office Action mailed 5/12/03, on pages 2-5 of the Office Action mailed 7/16/02, and for further reasons as discussed herein, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The arguments presented at pages 6-8 of the response are a reiteration of identical arguments set forth in the response filed November 30, 2004 at page 7, paragraph 4 through page 10, paragraph 3. Those arguments have already been addressed at pages 3-4 of the Office Action of 2/23/2005 and will not be reiterated here.

The only difference in Applicant's argument appears at page 8, lines 4-6 of the response where Applicant states "[a]s described in Example 15, Sprague-Dawley rats received six deposits of 0.3 μl sphere suspensions, wherein each suspension contained approximately 500,000 neural stem cells. (See Specification, page 31, lines 23-25)." This is highly misleading because, as discussed above, the cited section of the specification clearly discloses that the six deposits were **equivalent to** approximately 500,000 cells and that the cell suspension was used at a "final concentration of 250,000 cells/μl" (page 31, lines 10-12). However, Applicant's response of November 30, 2004 correctly acknowledged the teachings of Example 15 stating "[a]s described in Example 15, approximately 500,000 neural stem cells were transplanted into Sprague-Dawley rats. (See Specification, page 30, lines 23-25)" (see page 10, lines 4-6 of Applicant's response filed November 30, 2004).

At page 9, paragraph 1 of the response, Applicant asserts that the evidence of record confirms that transplantation of neural stem cells can be routinely achieved. Applicant further asserts that such transplantation results in a therapeutic benefit to the host. No support is offered for this assertion. While

non-therapeutic transplantation can be performed (i.e. cells may be implanted into the brain by a practitioner), protocols within the scope of the instantly claimed invention that produce a therapeutic effect were not available at the time of the invention, and given the state of the art, for reasons of record, undue experimentation would have been required to develop protocols within the scope of the claims that produce a therapeutic effect in a diseased animal.

At page 9, paragraph 2 of the response, Applicant asserts that the claimed method of transplantation would be useful as a restorative therapy for neurodegenerative diseases. Applicant further asserts that the evidence of record demonstrates that the improvement of delivering a mitogenic growth factor according to the claimed methods would also provide a therapeutic benefit to the host. No support is offered for these assertions, except to point broadly to the evidence of record. However, the evidence of record has already been addressed in detail in the prior Office Actions, particularly at pages 5-9 of the Office Action of 5/12/03 and pages 6-7 of the Office Action of 6/3/04.

At page 9, paragraph 3 of the response, Applicant again asserts, citing *In re Marzocchi*, that "it is incumbent upon the Patent Office, whenever a rejection for failure to teach how to make and/or use the claimed invention is made, to explain *why* it doubts the truth or accuracy of Applicant's statement and to back up any assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement" (emphasis original). In the instant case, ample reasons have been given to doubt that one skilled in the art could, using only routine experimentation as opposed to undue experimentation, use the claimed invention to produce a therapeutic effect. As detailed in the previous Office Actions, intensive investigation has been applied by many researchers, using a variety of protocols, in an effort to transplant neural stem cells, as well as other neural progenitor cells, to achieve a therapeutic effect. While the PTO bears the initial burden of providing reasons for doubting the objective truth of the statements made by Applicants as to the scope of enablement, when the PTO meets this burden, the burden shifts to Applicant to provide suitable evidence indicating that the specification is enabling in a manner

commensurate in scope with the protection sought by the claims. *In re Marzocchi*, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971).

At page 9, paragraph 4 of the response, Applicant asserts that "the Examiner merely relies on Jackowski (1995) British J. of Neurosurgery 9: 303-17 ("Jackowski") to support the enablement rejection. On the contrary, this is simply not true because the enablement rejection is based on Jackowski (1995), Milward et al. (1997), Mehler et al. (1999), Zhang et al. (1999), and Akiyama et al. (2001). See the enablement rejection set forth at pages 2-9 of the Office Action of 5/12/03.

At page 10, paragraph 1 of the response, Applicant warns that when evidence is submitted in rebuttal, the decision-maker must start over so that the entire path to decision is retracted and that facts established by rebuttal evidence must be evaluated along with the facts on which the earlier conclusions were reached, and not against the conclusion itself, such that a new decision will rest upon evaluation of the evidence as a whole. Contrary to Applicant's suggestion, the rebuttal evidence has been fully considered and addressed in detail in the prior Office Actions. Applicant's attention is particularly directed to pages 5-9 of the Office Action of 5/12/03, pages 6-7 of the Office Action of 6/3/04, and the enablement rejection set forth at pages 2-9 of the Office Action of 5/12/03 which clearly demonstrates that the rejection is based on the evidence as a whole, including the limited applicable working examples, the limited guidance provided in the specification, the broad scope of the claims with regard to the regions of the brain to be treated, and the unpredictability for achieving a therapeutic effect upon the transplantation of neural stem cells, in view of the state of the art. Thus, based upon the evidence as a whole, undue experimentation would have been required for one skilled in the art to practice the claimed method of the invnetion to achieve a therapeutic effect, the only real world utility asserted in the specification.

At page 10, paragraph 3 of the response, Applicants argue that they should not be held to the standard of having a perfected, commercially viable embodiment of the claimed invention. However, the

rejection of record is not based on and does not refer to a requirement for a perfected embodiment of the claimed invention, but rather only notes that, given the state of the art, for reasons of record, production of a therapeutic benefit would require undue experimentation. Applicants further assert that the post-filing references they have cited show that therapeutic benefit has been achieved using substantially identical methods to those disclosed in the instant application and that the improvement of delivering a mitogenic growth factor according to the claimed methods would also provide a therapeutic benefit to the host subject. However, Applicant provides no support for the assertion that the post-filing references used "substantially identical methods." These references have already been addressed in detail in the prior Office Actions and the evaluation reveals that the methods used were substantially different or that only healthy animals were used in the studies and therefore the experiments *could not* demonstrate a therapeutic effect. While post-filing references can be used to show that experiments performed in accordance with the teachings of the specification produced the necessary result, these are not that type of reference. Since the references are post-filing art that use protocols that differ substantially from the teachings of the instant specification, the skilled artisan would not have had the benefit of the teachings of these references at the time the instant application was filed.

Thus, the rejection under 35 U.S.C. 112, first paragraph, is maintained.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 6, 13, and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-3, 6, 13, and 14 are indefinite in their recitation of "selected from the group consisting of neurons, astrocytes, or oligodendrocytes" because it is unclear which cell types are necessarily

included in the group. Since the word "or" is used, the group need not include all 3 elements, but the term "consisting of" denotes a defined group. Use of the term "and" instead of "or" would be remedial.

Conclusion

No claims are allowed.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne-Marie Falk whose telephone number is (571) 272-0728. The examiner can normally be reached Monday through Friday from 10:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571) 272-0735. The central official fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Anne-Marie Falk, Ph.D.

Anne-Marie Falk
ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER